Report of a Leprosy case in Singapore: an age-old disease not to be forgotten in developed countries with low-prevalence settings

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Abstract

Introduction. Leprosy is rarely reported in developed countries with low-prevalence settings. Its diagnosis may be missed due to its low frequency in non-endemic regions, as well as its long incubation period. The report describes an imported leprosy case of a healthcare worker in Singapore.

Case presentation. A Filipino nursing personnel presented with a persistent non-tender erythematous plaque over his right upper back for many years despite topical treatment. He had the lesion before coming to Singapore but decided to seek medical consultation only after the lesion progressed with new erythematous papules developing over his face, trunk and upper limbs. Punch biopsies of skin lesions revealed fite-positive bacilli, which were identified to be Mycobacterium leprae by GenoType LepraeDR v1 assay (Hain LifeScience, Germany). No mutation was detected at rpoB (rifampicin), gyrA (ofloxacin) and folP1 (dapsone) gene targets. He was started on multi-drug therapy and responded to the treatment. The only prolonged close contact he had was his housemate who was screened and given a single dose of rifampicin as chemoprophylaxis.

Conclusion. In non-endemic settings, awareness is crucial in diagnosing leprosy. The availability of molecular testing and multi-disciplinary management are essential in the confirmation and control of this disease of public health importance.

INTRODUCTION

Leprosy, also known as Hansen’s disease, has been classified as a neglected tropical disease (NTD) by the World Health Organization (WHO) [1]. It is an infectious disease caused by Mycobacterium leprae and Mycobacterium lepromatosis and is often seen in the remote rural areas with tropical or subtropical conditions. Leprosy is rarely reported in developed countries [2], especially in low-prevalence settings such as Singapore. With increasing mobility of skilled migrants across the globe and international travel, however, patients with leprosy may present anywhere. Singapore is the melting pot of Asia with an influx of foreigners from nearby countries, which are endemic for leprosy. Though rare here, medical practitioners need to be aware of the possibility of leprosy and its presentation to avoid misdiagnosis. A high degree of clinical suspicion and the availability of laboratory diagnostic are required to make a correct diagnosis in this age-old disease of public health importance. Here, we report an imported case of leprosy in a healthcare worker in Singapore, which was confirmed by laboratory diagnosis. Informed consent for publication was obtained from the patient.

CASE REPORT

A Filipino male in his 30s presented with a persistent non-tender erythematous plaque over his right upper back for many years. It began as a faint erythema that slowly developed into a ring-like plaque lesion. It was non-pruritic in nature and the plaque did not respond to topical antifungal treatment. He had this skin lesion prior to arriving in Singapore but decided to seek medical attention as the lesion progressed with new erythematous papules developing over the face, trunk and upper limbs in the past 2 months. There was no prior trauma or irritants applied to the skin and the patient did not complain of any systemic symptoms of fever, loss of weight and night sweat. There was no numbness or weakness and he did not have another co-existing medical condition.
He denied ingestion of medication and sexual contact with a commercial sexual worker. The patient came to Singapore 7 years ago to work as nursing personnel and travelled back to the Philippines once to twice a year to visit his family. His housemate and family members did not have any skin complaint.

On physical examination, there was a large well demarcated annular plaque of 10 by 7.5 cm over the right upper back, which extended to the axilla (Fig. 1a). It was erythematous, infiltrated and not scaly. There were also multiple monomorphic papules of 0.5 to 1 cm in size over the upper limbs (Fig. 1b), face, proximal aspect of lower limbs and the gluteal region. Punch biopsies of the skin lesions were taken from the plaque at the back and one of the papules at the upper limb. Microscopic examination of the skin biopsies revealed a diffuse superficial dermal infiltrate of epithelioid histiocytes without well-formed granulomas surrounded by lymphocytes or any multinucleate Langhans giant cells. Foamy cytoplasm was seen in only a portion of the histiocytes and was subtle (Fig. 2a, b). Fite-positive bacilli were identified within the inflammatory infiltrate (Fig. 2c). All the controls demonstrated appropriate reactivity. In view of the histopathological findings, the microbiologists were consulted and deparaffinized samples from the skin lesions were sent for non-tuberculous mycobacteria (NTM) and leprosy molecular testing, which were performed using commercially available line-probe assays INNO-LiPA Mycobacteria v2 (Innogenetics, Belgium) and GenoType LepraeDR v1 (Hain LifeScience, Germany), respectively. The result was positive for *M. leprae* with no mutation detected at *rpoB* (rifampicin), *gyrA* (ofloxacin) and *folP1* (dapsone) gene targets by the assay.

The patient was followed up with the history and physical examination revisited. He came from a rural area with rice paddy fields and subsequently moved to the city to work. In Singapore, he worked in the operating theatre and assisted the anesthetist in intubation. A surgical mask and gloves were worn in the workplace at all times. He did not recall coming into contact with people suffering from leprosy. A detailed physical examination also revealed diminished sensation at the centre of the large annular indurated plaque over the right upper back and the ulnar nerves were mildly thickened bilaterally. Coarse facies was not noted. The patient was diagnosed to have borderline lepromatous leprosy and was counselled for the disease with the management explained. He was subsequently treated with multi-drug therapy (MDT) consisting of rifampicin, clofazimine and dapsone and responded to the treatment. The plaque and papules flattened with minimal induration. The case was notified to the relevant health authority and the infection control department in the

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**Fig. 1.** (a) A large well demarcated annular plaque of 10 by 7.5 cm over the right upper back, which extended to the axilla. (b) Multiple monomorphic papules of 0.5 to 1 cm in size over the right upper limb (bold arrows).

**Fig. 2.** (a) Skin punch biopsy from the right upper back plaque (H&E). (b) There is a diffuse superficial dermal infiltrate of epithelioid histiocytes without well-formed granulomas. Foamy cytoplasm was seen in only a portion of the histiocytes (H&E). (c) Fite-positive bacilli were observed within the inflammatory infiltrate (Fite stain).
respectively. The highest burden in the world is located at

[...]

LABORATORY diagnosis of leprosy can be challenging in a
topical treatment as seen in this case. The case also illustrated
of up to 2 decades [3]. Hence leprosy is still a possible differ-
maintenance vigilance and diagnostic capabilities for leprosy
in the developed countries with lower incidence as the world
becomes more connected with people travelling widely and
migrants moving from high-risk rural areas to the more
urbanized cities. In Singapore, leprosy is notifiable and the:

Although the incidence of leprosy is low in Singapore, clinical
vigilance and education remains important to avoid misdi-
agnosis. Heightened awareness is necessary as Singapore is
surrounded by countries that are endemic for leprosy. The
disease can present anywhere these days with the increase
in international travel and migration of skilled workers. This
case highlights the importance of clinical suspicion especially
in a patient whose native country is endemic for leprosy. It is
important to note that M. leprae has a long incubation period
of up to 2 decades [3]. Hence leprosy is still a possible differ-
ential in patients who have migrated for a number of years
and presents with atypical rashes that do not respond with
topical treatment as seen in this case. The case also illustrated
the importance of a multi-disciplinary team effort, which
involved dermatologists, histopathologists, microbiologists
and infection control practitioners in the diagnosis and
management of leprosy.

Laboratory diagnosis of leprosy can be challenging in a
low-prevalence setting as most laboratories do not have the
capability to test for the pathogen. Maintaining laboratory
expertise can be costly. Although the diagnosis of leprosy
is largely based on clinical findings and histology, the avail-
ability of molecular testing as a diagnostic tool can be useful
in confirming the clinical suspicion. Silt-skin smear, a semi-

classical and monitoring of treatment response in leprosy
cases, but skilled technicians are required to perform this
technique for reliable results [7].

Fite stain, on the other hand, is a useful special stain, which
is typically used in the histopathologic examination of fixed
tissue to examine for acid-fast organisms such as M. leprae. As
leprosy bacilli is less acid and alcohol fast than tubercle bacilli,
5% sulphuric acid is used in the decolourisation process in
place of an acid–alcohol solution. The process of deparaffi-
nization is also a delicate procedure. A mixture of peanut oil
and xylene is used to protect the cell wall from solvent and
the acid-fastness of M. leprae [8].

M. leprae is not cultivable in vitro except in animal models. It
is also not viable to perform susceptibility testing in a routine
diagnostic laboratory setting as the conventional method is to
inoculate the bacteria into a mouse footpad that requires a 1
year duration due to the long replication time of the pathogen
[7, 9]. It may only be performed in specialized laboratories with
animal facilities and is useful in viability studies, vaccine devel-
opment and the detection of new mutations [7, 9]. Molecular
techniques improve the detection rate of leprosy in the laboratory
setting greatly. Commercially available assays such as Geno-
Type LepraeDR (Hain LifeScience v1, Germany) are useful in
providing rapid identification and resistance profile genotypi-
cally [9]. It is a line-probe assay that utilizes DNA probes in
the detection of M. leprae and resistance to rifampicin, ofloxacin
dapsone in the same setting. This allows prompt diagnosis
to halt transmission and appropriate treatment to be initiated,
which decreases the risk of long-term sequelae. However, the
test is not cheap (~SGD 200) and can only be performed from
acid-fast bacilli (AFB) positive skin biopsies. Certain sub-types
and resistance not covered by the probes may potentially be
missed [10]. The advent of newer technology such as next
generation sequencing (NGS) will have an evolutionary role in
the diagnosis and control of leprosy. The knowledge of whole
genome sequences will enable molecular drug susceptibility to
be performed and potentially more resistance gene targets to be
identified. It will also allow detailed phyllogy to be performed,
which will be useful in the control of leprosy at large. Stefani
et al. have successfully utilized NGS to distinguish reinfection
from relapse in patients with recurrent leprosy and demonstrated
that treated leprosy cases can be reinfected by another strain in
endemic areas [11]. Such an application reveals how powerful
NGS can be in evaluating transmission dynamics and outcome.

Leprosy control is an ongoing effort involving education,
contact tracing and chemoprophylaxis. Droplet transmis-
sion is the likeliest mode of spread of the disease. WHO
recommended single-dose rifampicin (SDR) as the chemo-
 prophylactic intervention for contacts of leprosy cases [12].
The Public Health England (PHE) guideline mentioned
that household contacts should be traced and SDR may be
considered if the index case has multi-bacillary leprosy. Even
so, only about 5% of spouses of lepromatous cases develop
leprosy, which indicated that infection control precautions
are rarely required. Untreated leprosy patients do not require
isolation if they are admitted to healthcare facilities. Only
standard precautions are needed if they have open wounds or undergoing surgical procedures such as skin biopsies. *M. leprae* in the tissues are generally scanty and most are intracellular, degenerate and non-viable [13]. It was fortunate that our patient wore a surgical mask and gloves in his workplace, which minimized the risk of transmission.

To conclude, leprosy is still present in Singapore and it is important for clinicians to remain vigilant in order to diagnose the disease. Leprosy can happen anywhere including developed countries due to the high mobility of populations in current times and its long incubation period. Maintaining laboratory expertise remains relevant and molecular diagnostics expedite the testing in this slow-growing organism. A multi-disciplinary team effort is required to control this disease of public health importance.

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**Ethical statement**
Consent for publication was obtained from the patient.

**References**

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